

REMARKS

Claims 1-92 are pending in the subject application. Claims 1-47, and 82-92 are elected herein for initial prosecution, and claims 48-81 are withdrawn, in response to the current Restriction Requirement. Please note that claims 10 and 91, as currently amended, correct the omissions made in the previous claim listing (filed September 7, 2006). All elected claims 1-47, and 82-92, as currently amended, are believed to properly presented for examination.

By this Amendment, claims 1-4, 10-11, 15, 17-19, 24, 25, 32, 46, 82, 89, and 90-92 have been amended, and claims 5-9, 20-23, 26-29, 44, 47, and 83-88 have been canceled, for clarity in accordance with the Examiner's suggestions, without prejudice.

Entry of the foregoing amendments and reconsideration of the application in view of these amendments and accompanying remarks is respectfully requested.

Elections/Restrictions

There have been several Restriction Requirements rendered by the Office in the instant application. Following an Interview on November 20, 2006, the Office has now clarified restriction practice in this application, as set forth at page 2 of the Office Action. All prior Restriction Requirements levied by the Office are believed to be withdrawn and effectively stricken from the application.

The current Restriction Requirement renders a much simplified, two-way Restriction Requirement (Invention I, compositions; Invention II, methods), and a clarified species election requirement.

Pursuant to the Interview on November 20, 2006, and responsive to the new Restriction Requirement and species election requirement rendered in the instant Office Action, Applicant hereby elects Invention I, claims 1-47 and 82-92, drawn to permeabilizing peptides for enhancing mucosal paracellular transport and pharmaceutical compositions thereof. This election is made without prejudice, and Applicant reserves the right to prosecute the non-elected claims, and all other subject matter supported by the disclosure not presently under examination, in one or more related application(s).

Applicant further confirms the provisional election of species SEQ ID NO:4. Applicant reserves all rights of rejoinder with respect to this species election.

Because the previous Restriction Requirements, now withdrawn, prompted responsive amendments to the claims by Applicant, which amendments no longer pertain to the Restriction Requirement now presented, Applicant submits that the prior amendments to the claims should be also be considered withdrawn. Applicant has amended the claims accordingly herein consistent with the instant Restriction Requirement, which amendments properly reinstate certain subject matter previously withdrawn in response to earlier Restriction Requirements.

The current amendments also restructure the generic claims consistent with the instant Restriction Requirement, while at the same time clarifying the subject matter of these generic claims in accordance with Examiner's suggestions in the current Office Action, as discussed below. The current amendments modify the correct assignation of claims to which the elected species, SEQ ID NO: 4, reads upon. Examiner's detailed assignment of elected/withdrawn claims in this context (see Office Action at page 5) is believed to be obviated by the current amendments, and the elected species, SEQ ID NO: 4, is believed to read on all of the claims now presented within elected Group I.

#### Patentability Under 35 U.S.C. § 101

Claims 82-84, 87, 89, 91 and 92 are rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. Examiner asserts that these claims read on naturally occurring proteins, e.g., JAM-1, principally because the claimed peptides are allegedly not limited in length.

All of the claims as currently amended present finite peptide length limitations that clearly distinguish the subject peptides from naturally occurring proteins, thereby obviating this rejection.

#### Claim Objections

Claims 10, 15, 17, 32 and 91 are objected to based on various alleged informalities presented at pp. 6-7 of the Office Action. Applicant has made appropriate corrections in accordance with the Examiner's suggestions to remedy each of these objections.

Patentability Under 35 U.S.C. § 112

Claims 1-5, 10-17, 30-47, 82-84, 87, 89, 91 and 92 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The authority and reasoning relied upon to support this rejection is presented at pp. 7-11 of the Office Action. Principally, the Examiner contends that “most claims do not provide structure, but rather rely on the function.” With regard to the subject peptides, the Examiner states that “[t]he peptidic element must function as a permeabilizing peptide, however no specific structural element is coupled to function.” Similar objections are stated with respect to “additional elements, e.g., ciliostatic agent, vasodilatory agent . . . .”

Applicant has amended the claims herein to incorporate structural details for each of the claimed permeabilizing peptides, and to further clarify the relationship between these structural details and the function of the peptides as permeabilizing peptides. These amendments are respectfully submitted to overcome the instant rejection as it pertains to permeabilizing peptides.

With regard to the “additional elements” alluded to by Examiner, all such elements presented in the instant claims are believed to fully comply with the written description requirement. The sole requirement in this context is that the claims, read in light of the specification, must “reasonably convey” the subject matter of the invention to persons of ordinary skill in the art. This requirement must further be considered in light of the primary subject matter of the invention—namely compositions and methods employing permeabilizing peptides for enhancing mucosal delivery of a range of “biologically active agents.” Applicant has described and exemplified the nature and scope of these biologically active agents extensively throughout the specification.

Examining dependent claim 13, for example, the biologically active agent may be selected from such agents as:

an opiod, opiod antagonist, corticosterone, anti-inflammatory, androgen, estrogen, progestin, muscle relaxant, vasodilator, antihistamine, histamine receptor site blocking agent, antitussive, antiepileptic, anti-fungal agent, antibacterial agent, cancer therapeutic agent, antioxidant, antiarrhythmic agents, antihypertensive agent, monoclonal or polyclonal antibody,

anti-sense oligonucleotide, and an RNA, DNA or viral vector comprising a gene encoding a therapeutic peptide or protein.

Each of these groups of biologically active agents, despite their recitation here in terms construed by the Examiner as primarily “functional”, actually corresponds to well defined subject matter. The nature and scope, for example, of an “antihistamine”, or an “antihypertensive agent” is fully elucidated by the disclosure, supplemented by knowledge in the art, in a manner which comprehends specific, structurally well characterized examples of compounds within each of the subject groups. These references, relating to dependent aspects of the invention, are in fact conventional and it would be unduly burdensome and contrary to standards of practice to import all species comprehended within each contemplated group into the body of the claims.

In view of the foregoing, the rejection of claims 1-5, 10-17, 30-47, 82-84, 87, 89, 91 and 92 under 35 U.S.C. § 112, first paragraph, is respectfully submitted to be overcome.

Claims 44 and 47 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. Without acceding to the merits of this rejection, Applicant notes that the rejection is obviated by cancellation of claims 44 and 47, without prejudice, herein.

Claims 1-5, 10-17, 30-47, 82-84, 87, 89, 91 and 92 are rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. Applicant has amended the claims to address each of the asserted grounds for rejection, and withdrawal of the rejection is earnestly solicited.

#### Patentability Under 35 U.S.C. § 102

Claims 82-84, 87, 89, 91 and 92 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Liu, et al., *J. Cell Sci.* 113:2363-2374, 2000. Liu, et al., is cited for allegedly teaching full length human JAM-1 protein, which the Examiner states “comprises the sequence VRIP and comprises from about 4-25 contiguous residues of the extracellular domain of JAM-1. The Examiner further asserts that the term “reference sequence” is not defined, and that this alleged deficiency relates to the construction of Liu as reading on the instant claims.

The amendments to the claims herein, including recitation of a specific length range of the claimed permeabilizing peptides, clearly distinguish the subject matter of the claims over the

alleged disclosure by Liu of a full length human JAM-1 protein. Withdrawal of this rejection is thereby respectfully requested.

Claims 82-84, 91 and 92 are rejected under 35 USC § 102(b) as allegedly anticipated by Blaszczyk-Thurin (WO 00/27420 A1). This reference is cited for allegedly teaching SEQ ID NO: 119 (GLDLLGDVRIPVVRR). This peptide is construed by the Examiner as teaching “a peptide which comprises about 4 contiguous residues of JAM-1 with one or more addition/substitution/deletion [*sic*] of JAM-1.”

The amendments to the claims herein, including withdrawal, without prejudice, of addition/substitution/deletion variants of the claimed VRIP peptide, clearly distinguish the subject matter of the rejected claims over the alleged teaching by Blaszczyk-Thurin of SEQ ID NO: 119 (GLDLLGDVRIPVVRR). Withdrawal of this rejection is thereby respectfully requested.

Claims 1-5, 12-14, 16, 17, 32-41 and 82-84 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Blaschuk (U.S. Patent No. 6,391,855). This reference is cited for allegedly teaching “a JAM peptide comprising JAM CAR sequence SFTIDPKSG (SEQ ID NO: 2) (claim 1) in a pharmaceutical composition with a pharmaceutically acceptable carrier (claim 9) and a drug (claim 10).” Examiner further asserts that:

In looking to the specification, Blaschuk teaches that ‘virtually any drug may be administered in combination with a modulating agent as described herein’ (column 23, lines 51-52) and provides a myriad of drugs that can be used, including taxol, mitomycin C, indomethacin and ibuprofen, as well as generic antifungals, analgesics, vasodilators, narcotic antagonists (e.g., column 23 line 53 to column 24, line 6). The peptide of Blaschuk is an extracellular domain of murine JAM.

The amendments to the claims herein, including withdrawal, without prejudice, of addition/substitution/deletion variants of the claimed peptide relating to SFTIDPKSG (SEQ ID NO: 2), clearly distinguish the subject matter of the rejected claims over the alleged teaching by Blaschuk. Withdrawal of this rejection is thereby respectfully requested.

Patentability Under 35 U.S.C. § 103

Claims 1-5, 10-13, 17, 30-46, 82-84, 87, 89, 91 and 92 are rejected under 35 USC § 103(a) as allegedly obvious over Liu et al., as applied to claims 82-84, 8, 89, 91 and 92 above, in view of Quay (US 2004/0028613 A1).

The deficiencies of Liu, et al., as pertaining to the subject matter of the currently-amended claims are discussed above. These deficiencies fail to support construction of Liu, et al., as a primary reference, in combination with Quay, to render the subject matter of claims 1-5, 10-13, 17, 30-46, 82-84, 87, 89, 91 and 92 obvious as alleged. Withdrawal of this rejection is thereby respectfully requested.

Claims 1-5, 10-13, 17, 30-46, 82-84, 87, 89, 91 and 92 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Liu et al., as applied to claims 82-84, 8, 89, 91 and 92 above, in view of Quay (US 2004/0028613 A1).

The deficiencies of Liu et al. as pertaining to the subject matter of the currently-amended claims are discussed above. These deficiencies fail to support construction of Liu, et al., as a primary reference, in combination with Quay, to render the subject matter of claims 1-5, 10-13, 17, 30-46, 82-84, 87, 89, 91 and 92 obvious as alleged. The deficiencies of Quay in this context are also apparent, including the notation by the Examiner that “Quay does not specifically teach JAM-1.”

Applicant further reserves the right to challenge the prior art status of Quay as applied by Examiner, by a showing under either or both 37 C.F.R. 1.132 and 37 C.F.R. 1.131

In view of the foregoing, the rejection of claims 1-5, 10-13, 17, 30-46, 82-84, 87, 89, 91 and 92 under 35 U.S.C. § 103(a) as allegedly obvious over Liu, et al., in view of Quay is respectfully submitted to be overcome.

Claims 1-5, 12-17, 32-44, 47 and 82-84 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Blaschuk, as applied to claims 1-5, 12-14, 16, 17, 32-41 and 82-84 above, in view of Platz (U.S. Patent No. 5,345,562).

The deficiencies of Blaschuk as pertaining to the subject matter of the currently-amended claims are discussed above. These deficiencies fail to support construction of Blaschuk, as a primary reference, in combination with Platz, to render the subject matter of claims 1-5, 12-17,

32-44, 47 and 82-84 obvious as alleged. Accordingly, this rejection is respectfully submitted to be overcome.

Double Patenting

Various provisional double patenting rejections are set forth at pp. 19-21 of the Office Action. Applicant notes the provisionality of these rejections and will take appropriate action to address these rejections upon allowance of claims in one of the subject applications.

At pp. 21-22 of the Office Action, Examiner presents comments relating to presentation of subject matter which is allegedly "not patentably distinct" in various copending applications commonly assigned with the present case. Applicant believes that the current amendments to the claims preclude this assessment, and clarification by the Office of the status of respective claims in the cited applications on this basis is earnestly solicited. Applicant reserves the right to further address this issue by a showing under 35 U.S.C. § 103(c) and/or 37 C.F.R. § 1.78(c), clarifying ownership and/or inventorship among the allegedly conflicting applications.

It is believed that no fee is required for this submission. Should, however, the U.S. Patent and Trademark Office determine that any fee is due or that a refund is owed for this application, the Commissioner is hereby authorized and requested to charge the required fee and/or credit the refund owed to our Deposit Account No. 502769.

Respectfully submitted,  
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